Suggested Reading

Patent Foramen Ovale References

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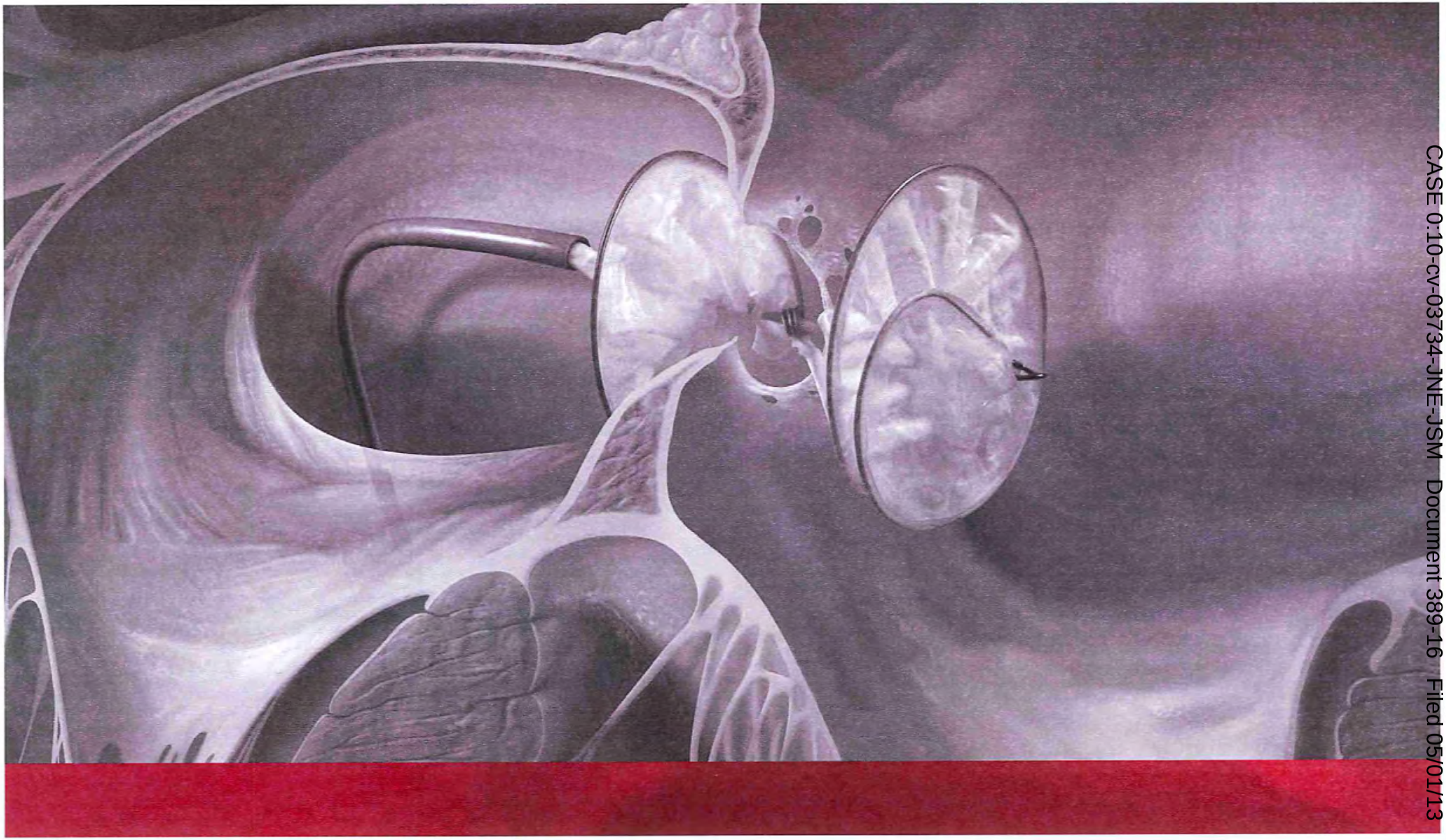

SELECTED DATA FROM THE FDA CLINICAL TRIAL

GORE HELEX SEPTAL OCCLUDER

AGA_GORE0442741
G-1

Selected Data from the US Clinical Trial

ADVERSE EVENTS

Three US clinical studies were conducted to evaluate the GORE HELEX Septal Occluder. These studies were performed with the original delivery system. The product described in the *Instructions for Use* is the same Occluder with a modified delivery system. Please note that the modified delivery system was not evaluated under the original US clinical study.

The GORE HELEX Septal Occluder was evaluated in a Feasibility Study (two center, single arm), a Pivotal Study (multi-center, non-randomized), and a Continued Access Study (multi-center, single arm, prospective). The Feasibility Study included 51 subjects treated with the device. The Pivotal Study compared the device to surgical closure of *ostium secundum* atrial septal defects. Investigators were required to complete three device training cases. The Pivotal Study included 119 non-training subjects treated with the device and 128 subjects treated with surgical closure. The Continued Access Study included 137 non-training subjects treated with the device as of August 1, 2006, of which 122 subjects completed the 12 month follow-up evaluation.

These subjects form the basis of the observed adverse event data reported in the following section. An independent Data Safety Monitoring Board (DSMB) reviewed all reported adverse events to determine device / procedure relationship and event severity (major or minor). An event was considered major if it required reintervention, readmission to the hospital or resulted in permanent damage or deficit. For the GORE HELEX Septal Occluder studies, reintervention was defined as chronic medical, and acute surgical or interventional cardiology therapies.

Deaths

There was one post-operative death in the surgical control treatment arm of the Pivotal Study. Subject died of complications related to post-pericardiotomy syndrome on Day 10 post-surgery. No deaths have been reported in the device subjects in the Feasibility, Pivotal, or Continued Access Studies.

Observed Adverse Events

Major adverse events reported through the 12 month follow-up for the Feasibility, Pivotal and Continued Access Studies are presented in Table G-1.

GORE HELEX SEPTAL OCCLUDER

Consult Instructions for Use

Major Adverse Events

Table G-1

Number of Subjects with Successful Device Delivery by Category of Major Adverse Events — GORE HELEX Septal Occluder Studies Events Reported Through 12 Month Follow-up

		Pivotal Study			Continued Access Study
	Feasibility Study	Device Arm	Surgery Arm	Difference (95% CI)[1]	
Subjects Evaluable for Safety	**51**	**119**	**128**		**137**
Deaths (Any Cause)	**0**	**0**	**1 (0.8%)**	**-0.8% (-2.4%, 0.8%)**	**0**
Subjects With One or More Major Adverse Events	**2 (3.9%)**	**7 (5.9%)**	**14 (10.9%)**	**-5.1% (-12.1%, 1.9%)**	**3 (2.2%)**
Cardiac	**1 (2.0%)**	**2 (1.7%)**	**10 (7.8%)**	**-6.1% (-11.5%, -0.8%)**	**2 (1.5%)**
Arrhythmia	1 (2.0%)	0	0		0
Bleeding (treatment required)	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Device Embolization (post-procedure)[2]	0	2 (1.7%)	n / a	n / a	2 (1.5%)
Pulmonary Edema	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Post-Pericardiotomy Syndrome	n / a	n / a	8 (6.3%)		n / a
Integument (Skin)	**0**	**1 (0.8%)**	**0**	**0.8% (-0.8%, 2.4%)**	**0**
Allergic Reaction	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Neurologic	**1 (2.0%)**	**2 (1.7%)**	**0**	**1.7% (-0.6%, 3.9%)**	**0**
Migraine (new)	0	2 (1.7%)	0	1.7% (-0.6%, 3.9%)	0
Paresthesia	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Seizure	1 (2.0%)	0	0		0
Pulmonary (Respiratory)	**0**	**0**	**1 (0.8%)**	**-0.8% (-2.4%, 0.8%)**	**0**
Stridor	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Vascular	**0**	**1 (0.8%)**	**1 (0.8%)**	**0.1% (-2.2%, 2.3%)**	**0**
Hemorrhage (treatment or intervention required)	0	1 (0.8%)	1 (0.8%)	0.1% (-2.2%, 2.3%)	0
Wound	**0**	**0**	**2 (1.6%)**	**-1.6% (-3.8%, 0.7%)**	**0**
Hernia	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Scarring or Scar Related	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Device (GORE HELEX Septal Occluder)	**0**	**3 (2.5%)**	**n / a**	**n / a**	**1 (0.7%)**
Allergic Reaction	0	1 (0.8%)	n / a	n / a	0
Device Size Inappropriate	0	2 (1.7%)	n / a	n / a	0
Device Removal Due to Fracture	0	0	n / a	n / a	1 (0.7%)
Other	**0**	**0**	**1 (0.8%)**	**-0.8% (-2.4%, 0.8%)**	**0**
Anemia	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0

NOTE: Analysis includes all Feasibility subjects, non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006 and evaluated through 12 month follow-up.

n / a: Not applicable

[1] Differences between Pivotal device and surgery groups and associated 95% confidence intervals.

[2] The four embolized devices were removed by transcatheter technique.

Consult Instructions for Use

GORE HELEX SEPTAL OCCLUDER

Minor Adverse Events

Table G-2a

Number of Subjects with Successful Device Delivery by Category of Minor Adverse Events — GORE HELEX Septal Occluder Studies Events Reported Through 12 Month Follow-up

	Pivotal Study				Continued Access Study
	Feasibility Study	Device Arm	Surgery Arm	Difference (95% CI)[1]	
Subjects Evaluable for Safety	**51**	**119**	**128**		**137**
Subjects With One or More Minor Adverse Events	**19 (37.3%)**	**34 (28.6%)**	**36 (28.1%)**	**0.4% (-10.9%, 11.8%)**	**46 (33.6%)**
Cardiac	**7 (13.7%)**	**14 (11.8%)**	**26 (20.3%)**	**-8.5% (-17.8%, 0.7%)**	**7 (5.1%)**
Arrhythmia	3 (5.9%)	10 (8.4%)	5 (3.9%)	4.5% (-1.5%, 10.5%)	4 (2.9%)
Chest Pain	1 (2.0%)	2 (1.7%)	0	1.7% (-0.6%, 3.9%)	0
Embolus – Air	1 (2.0%)	0	2 (1.6%)	-1.6% (-3.8%, 0.7%)	0
Hemopericardium	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Hypotension	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Other – Cardiac Complication	0	0	0		1 (0.7%)
Palpitations	1 (2.0%)	0	0		1 (0.7%)
Pericardial Effusion	1 (2.0%)	1 (0.8%)	5 (3.9%)	-3.1% (-6.9%, 0.8%)	1 (0.7%)
Pneumopericardium	0	0	3 (2.3%)	-2.3% (-5.1%, 0.4%)	0
Post-Pericardiotomy Syndrome	n / a	n / a	10 (7.8%)		n / a
Syncope	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Vaso-Vagal Reaction	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Integument	**0**	**0**	**0**		**1 (0.7%)**
Abrasion	0	0	0		1 (0.7%)
Musculo-Skeletal	**0**	**0**	**0**		**1 (0.7%)**
Chest Pain	0	0	0		1 (0.7%)
Neurologic	**7 (13.7%)**	**8 (6.7%)**	**0**	**6.7% (2.3%, 11.1%)**	**17 (12.4%)**
Dizziness	2 (3.9%)	0	0		0
Headache	4 (7.8%)	5 (4.2%)	0	4.2% (0.7%, 7.7%)	15 (10.9%)
Migraine (pre-existing)	0	0	0		2 (1.5%)
Migraine (new)	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	1 (0.7%)
Paresthesia	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Visual Field Disturbance or Defect	1 (2.0%)	2 (1.7%)	0	1.7% (-0.6%, 3.9%)	0
Pulmonary (Respiratory)	**0**	**1 (0.8%)**	**8 (6.3%)**	**-5.4% (-10.1%, -0.7%)**	**1 (0.7%)**
Atelectasis	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Congestion	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Dyspnea	0	0	0		1 (0.7%)
Pleural Effusion (not requiring drainage)	0	0	3 (2.3%)	-2.3% (-5.1%, 0.4%)	0
Pneumothorax	0	0	4 (3.1%)	-3.1% (-6.3%, 0.0%)	0
Pneumonia	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0

Minor adverse events reported through the 12 month follow-up for the Feasibility, Pivotal and Continued Access Studies are presented in Table G-2a and Table G-2b.

NOTE: Analysis includes all Feasibility subjects, non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006 and evaluated through 12 month follow-up.

n / a: Not applicable

[1] Differences between Pivotal device and surgery groups and associated 95% confidence intervals.

Consult Instructions for Use

GORE HELEX SEPTAL OCCLUDER

Minor Adverse Events (continued)

Table G-2b

Number of Subjects with Successful Device Delivery by Category of Minor Adverse Events — GORE HELEX Septal Occluder Studies Events Reported Through 12 Month Follow-up

		Pivotal Study			Continued Access Study
	Feasibility Study	Device Arm	Surgery Arm	Difference (95% CI)[1]	
Renal and Uro-Genital	**0**	**1 (0.8%)**	**0**	**0.8% (-0.8%, 2.4%)**	**0**
Urinary Retention	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Anesthesia	**1 (2.0%)**	**3 (2.5%)**	**1 (0.8%)**	**1.7% (-1.4%, 4.9%)**	**7 (5.1%)**
Abdominal Pain	0	0	0		1 (0.7%)
Bleeding (no treatment required)	0	0	0		1 (0.7%)
Corneal Abrasion	0	0	0		1 (0.7%)
Emesis	0	1 (0.8%)	1 (0.8%)	0.1% (-2.2%, 2.3%)	1 (0.7%)
Nausea	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Nausea with Emesis	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	4 (2.9%)
Paresthesia	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Sore Throat	1 (2.0%)	0	0		0
Drug-Related	**5 (9.8%)**	**6 (5.0%)**	**2 (1.6%)**	**3.5% (-1.0%, 7.9%)**	**7 (5.1%)**
Allergic Response	1 (2.0%)	0	2 (1.6%)	-1.6% (-3.8%, 0.7%)	0
Bruising / Ecchymosis	2 (3.9%)	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	4 (2.9%)
Gastric Irritation	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	0
Nosebleed	1 (2.0%)	4 (3.4%)	0	3.4% (0.2%, 6.5%)	3 (2.2%)
Rectal Bleeding	1 (2.0%)	0	0		0
Wound	**2 (3.9%)**	**1 (0.8%)**	**4 (3.1%)**	**-2.3% (-5.8%, 1.3%)**	**3 (2.2%)**
Access Site Bleeding	0	1 (0.8%)	0	0.8% (-0.8%, 2.4%)	1 (0.7%)
Access Site Pain	1 (2.0%)	0	0		0
Hematoma (not requiring treatment or intervention)	1 (2.0%)	0	0		2 (1.5%)
Scarring or Scar Related	0	0	2 (1.6%)	-1.6% (-3.8%, 0.7%)	0
Suture Related	0	0	1 (0.8%)	-0.8% (-2.4%, 0.8%)	0
Sternal Wire	n / a	n / a	1 (0.8%)		n /a
Delivery System	**2 (3.9%)**	**1 (0.8%)**	**n / a**	**n / a**	**0**
Tan Mandrel Kink	1 (2.0%)	0	n / a	n / a	0
Retrieval Cord Break	1 (2.0%)	0	n / a	n / a	0
Retrieval Cord Detachment	0	1 (0.8%)	n / a	n / a	0
Device (GORE HELEX Septal Occluder)	**3 (5.9%)**	**6 (5.0%)**	**n / a**	**n / a**	**10 (7.3%)**
Fracture-Wire Frame	3 (5.9%)	6 (5.0%)	n / a	n / a	10 (7.3%)
Non-Investigational Device Related	**0**	**0**	**0**		**1 (0.7%)**
Contrast Reaction	0	0	0		1 (0.7%)
Other	**0**	**0**	**0**		**3 (2.2%)**
Fever	0	0	0		1 (0.7%)
Nosebleed	0	0	0		1 (0.7%)
Other	0	0	0		1 (0.7%)

Minor adverse events reported through the 12 month follow-up for the Feasibility, Pivotal and Continued Access Studies are presented in Table G-2a and Table G-2b.

NOTE: Analysis includes all Feasibility subjects, non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006 and evaluated through 12 month follow-up.

n / a: Not applicable

[1] Differences between Pivotal device and surgery groups and associated 95% confidence intervals.

Consult Instructions for Use

GORE HELEX SEPTAL OCCLUDER

Clinical Summary

Three US clinical studies were conducted to evaluate the GORE HELEX Septal Occluder. These studies were performed with the original delivery system. The product described in the *Instructions for Use* is the same Occluder with a modified delivery system. Please note that the modified delivery system was not evaluated under the original US clinical study.

Feasibility Study

The GORE HELEX Septal Occluder was evaluated in a single arm, prospective Feasibility Study intended to provide an initial evaluation of the safety and performance of the GORE HELEX Septal Occluder for closure of *ostium secundum* atrial septal defects (ASDs). Two US sites participated in the study and enrolled 63 subjects. The median subject age was 11 years (range: 6 months to 65 years) and 65% of the subjects were female. The median estimated defect size was 12 mm (range: 4.5 to 20 mm), in subjects with a delivery attempt (n = 59), the median stretched defect size was 18 mm (range 6 to 26 mm).

The GORE HELEX Septal Occluder was successfully implanted in 86.4% (51 / 59) of subjects with a delivery attempt. Subjects with a successful device delivery were followed for 12 months. No deaths, device embolizations, thrombus on the device, or erosions requiring surgery were reported through the 12 month follow-up. There were no repeat procedures to the target ASD in the study population.

Of subjects evaluated for 12 month ASD closure by independent echocardiography core laboratory review, 94.6% (35 / 37) had a successful defect closure (complete occlusion or clinically insignificant leak). Clinically significant leaks were present in two subjects (5.4%) at the 12 month follow-up evaluation. Clinical success, a composite of safety (no major adverse events or repeat procedure) and efficacy (clinical closure at 12 months), was achieved in 89.5% of subjects (34 / 38) available for evaluation.

Table G-3

GORE HELEX Septal Occluder Feasibility Study Principal Safety and Effectiveness Results	FEASIBILITY
Technical Success[1]	51 / 59 (86.4%)
Clinical Closure Success[2]	
Pre-Discharge	49 / 51 (96.1%)
6 Months	30 / 31 (96.8%)
12 Months	35 / 37 (94.6%)
Principal Safety Measures	
Major Adverse Events 12 Months	2 / 51 (3.9%)
Minor Adverse Events 12 Months	19 / 51 (37.3%)
Survival at 365 Days (K-M)	100%
Composite Clinical Success 12 Months[3]	34 / 38 (89.5%)

1 Technical Success defined as successful delivery of the device.
2 Clinical Closure Success defined as defect that is either Completely Occluded or Clinically Insignificant Leak. Leak status was evaluated by the investigational sites at pre-discharge and 6 months and by the echocardiography core laboratory at 12 months.
3 Composite Clinical Success defined as no major adverse event or repeated procedure and clinical closure success at 12 months.

Consult Instructions for Use

GORE HELEX SEPTAL OCCLUDER

Pivotal and Continued Access Studies

PURPOSE

The purpose of the Pivotal Study was to evaluate the safety and effectiveness of the GORE HELEX Septal Occluder for the closure of *ostium secundum* atrial septal defects. The purpose of the Continued Access Study was to evaluate design modifications to the GORE HELEX Septal Occluder. The design modifications incorporated into the GORE HELEX Septal Occluder were implemented based on investigator input and feedback given during the Feasibility and Pivotal Trials.

Consult Instructions for Use

GORE HELEX SEPTAL OCCLUDER

Patient Selection

PIVOTAL STUDY

The Pivotal Study enrolled 143 non-training subjects in the device treatment arm and 128 subjects in the surgical control arm at 14 clinical sites within the US. Investigators who did not participate in the Feasibility Study were required to complete three device training cases. Fifty subjects were enrolled as training cases and these subjects were excluded from the primary endpoint analyses.

Enrolled patients had echocardiographic evidence of an *ostium secundum* atrial septal defect and right heart volume overload (or as indicated by a Q_P:Q_S ratio of ≥ 1.5:1 for the device treatment arm). Patients enrolled in the device treatment arm had a defect size of 22 mm or less as measured by balloon sizing and an adequate rim to retain the device present in ≥ 75% of the circumference of the defect. Patients enrolled in the surgical control arm had surgical intervention within 12 months of IRB approval for the study, a minimum body weight of 8 kg at the time of surgery, and a pre-operative, non-anesthesized echocardiogram performed within six months of the ASD surgery date. Exclusion criteria included:

- Patient had concurrent cardiac defect(s) that were associated with potentially significant morbidity or mortality that could elevate morbidity / mortality beyond what is common for ASD or that is expected to require surgical treatment within two years for the device treatment group or five years for the surgical control group.
- Patient had systemic or inherited conditions that would significantly increase patient risk of major morbidity and mortality during the term of the study.
- Patient had an uncontrolled arryhthmia.
- Patient had history of stroke.
- Patient was pregnant or lactating.
- Patient had contraindication to antiplatelet therapy (device treatment arm).
- Patient had a pulmonary artery systolic pressure greater than half the systemic systolic arterial pressure unless the indexed pulmonary artery resistance was < 5 Woods units (device treatment arm).
- Patient had significant atrial septal aneurysm (device treatment arm).
- Patient had multiple defects that would require placement of greater than one device (device treatment arm).
- Patient had an atrial septum > 8 mm thick (device treatment arm).
- Patient had an attempted transcatheter septal defect closure device placement within one month of surgery (surgical control arm).
- Patient had significant pulmonary hypertension at the time of surgery (surgical control arm).
- Patient had already completed a routine 12 month post-operative evaluation (surgical control arm).

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GORE HELEX SEPTAL OCCLUDER

Continued Access Study

The Continued Access Study enrolled 189 non-training subjects at 13 clinical sites within the US as of August 1, 2006. Investigators who did not participate in the Feasibility and Pivotal Studies were required to complete three device training cases and these cases were excluded from the primary analyses. Enrolled subjects met the same inclusion and exclusion criteria as the Pivotal Study subjects.

GORE HELEX SEPTAL OCCLUDER

Consult Instructions for Use

Demographics

The median age of the 143 subjects enrolled in the device treatment arm of the Pivotal Study was 6.5 years (range: 1.4 to 72.4 years) and 65.7% of the subjects were female. The median estimated defect size was 10 mm (range: 1.3 to 25 mm) and in subjects with a delivery attempt (n = 134), the median stretched defect size was 14 mm (range 5 to 24 mm).

The median age of the 128 subjects enrolled in the surgical control arm of the Pivotal Study was 4.7 years (range: 0.6 to 70.4 years), and 63.3% of the subjects were female. The median estimated defect size was 15 mm (range: 1.5 to 42 mm).

The median age of the 189 non-training subjects enrolled in the Continued Access Study was 5.4 years (range: 0.8 to 58.4 years) and 65.6% of the subjects were female. The median estimated defect size was 10.0 mm (range: 1.7 to 21.0 mm). In subjects with a delivery attempt (n = 160), the median stretched defect size was 14.0 mm (range: 4.5 to 22 mm).

Subject Demographics

Table G-4

GORE HELEX Septal Occluder Studies — Subject Demographics				
	Pivotal Study			Continued Access Study
	Device Arm	Surgery Arm	Difference (95% CI)[1]	
Number of Subjects	**143**	**128**		**189**
Gender				
Male	49 (34.3%)	47 (36.7%)	-2.5% (-13.9%, 9.0%)	65 (34.4%)
Female	94 (65.7%)	81 (63.3%)	2.5% (-9.0%, 13.9%)	124 (65.6%)
Subject Ethnicity				
White or Caucasian	95 (66.4%)	84 (65.6%)	0.8% (-10.5%, 12.1%)	131 (69.3%)
Black or African American	15 (10.5%)	9 (7.0%)	3.5% (-3.2%, 10.2%)	13 (6.9%)
Hispanic or Latino	26 (18.2%)	23 (18.0%)	0.2% (-9.0%, 9.4%)	23 (12.2%)
Asian	3 (2.1%)	7 (5.5%)	-3.4% (-8.0%, 1.2%)	7 (3.7%)
Other	3 (2.1%)	3 (2.3%)	-0.2% (-3.8%, 3.3%)	11 (5.8%)
Unknown	1 (0.7%)	2 (1.6%)	-0.9% (-3.4%, 1.7%)	4 (2.1%)
Subject Age (years)				
N	143	128		189
Mean (Std Dev)	12.4 (14.0)	9.2 (12.2)	3.2 (0.1, 6.4)	8.9 (9.6)
Median	6.5	4.7		5.4
Range	(1.4, 72.4)	(0.6, 70.4)		(0.8, 58.4)
Weight (kg)				
N	143	128		189
Mean (Std Dev)	35.6 (26.0)	27.5 (22.4)	8.2 (2.3, 14.0)	29.3 (22.3)
Median	23.0	17.5		19.0
Range	(9.2, 132.5)	(8.3, 135.0)		(6.9, 114.0)
Body Surface Area (BSA)				
N	143	128		189
Mean (Std Dev)	1.08 (0.51)	0.91 (0.46)	0.2 (0.1, 0.3)	0.95 (0.47)
Median	0.89	0.72		0.77
Range	(0.32, 2.61)	(0.38, 2.01)		(0.33, 2.40)
Estimated ASD Size (mm)				
N	141	124		188
Mean (Std Dev)	10.7 (3.8)	15.5 (6.3)	-4.8 (-6.1, -3.6)	10.0 (3.2)
Median	10.0	15.0		10.0
Range	(1.3, 25.0)	(1.5, 42.0)		(1.7, 21.0)

NOTE: Analysis includes all Feasibility subjects, non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006 and evaluated through 12 month follow-up.

[1] Differences between Pivotal device and surgery groups and associated 95% confidence intervals.

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GORE HELEX SEPTAL OCCLUDER

Subject Medical History

Table G-5

GORE HELEX Septal Occluder Studies — Subject Medical History				
	Pivotal Study			Continued Access Study
	Device Arm	Surgery Arm	Difference (95% CI)[1]	
Subjects Enrolled	**143**	**128**		**189**
General Medical History				
Previous Cardiac Surgery	8 (5.6%)	4 (3.1%)	2.5% (-2.4%, 7.3%)	9 (4.8%)
ECG Abnormalities	72 (50.3%)	89 (69.5%)	-19.2% (-30.6%, -7.7%)	109 (57.7%)
Cardiac Arrhythmia(s)	12 (8.4%)	3 (2.3%)	6.0% (0.8%, 11.3%)	7 (3.7%)
Chromosomal Abnormalities	4 (2.8%)	7 (5.5%)	-2.7% (-7.4%, 2.1%)	16 (8.5%)
Emotional or Psychiatric Problems	5 (3.5%)	0 (0.0%)	3.5% (0.5%, 6.5%)	7 (3.7%)
Epilepsy	0 (0.0%)	0 (0.0%)	0.0% (0.0%, 0.0%)	2 (1.1%)
Failure to Thrive	1 (0.7%)	5 (3.9%)	-3.2% (-6.8%, 0.4%)	8 (4.2%)
Migraines	3 (2.1%)	1 (0.8%)	1.3% (-1.5%, 4.1%)	3 (1.6%)
Neurological Deficits / Symptoms	7 (4.9%)	5 (3.9%)	1.0% (-3.9%, 5.9%)	9 (4.8%)
Other (non-ASD) Cardiac Disease	15 (10.5%)	5 (3.9%)	6.6% (0.5%, 12.6%)	22 (11.6%)
Other Vascular Disease	2 (1.4%)	1 (0.8%)	0.6% (-1.8%, 3.1%)	3 (1.6%)
Pre-Term Baby	6 (4.2%)	8 (6.3%)	-2.1% (-7.4%, 3.3%)	15 (7.9%)
Respiratory Difficulties	14 (9.8%)	13 (10.2%)	-0.4% (-7.5%, 6.8%)	23 (12.2%)
Hepatitis	0 (0.0%)	0 (0.0%)		0 (0.0%)
Other	29 (20.3%)	43 (33.6%)	-13.3% (-23.8%, -2.8%)	79 (41.8%)
Current Medication				
Anti-Arrhythmic	7 (4.9%)	2 (1.6%)	3.3% (-0.8%, 7.5%)	0 (0.0%)
Anti-Coagulant	2 (1.4%)	0 (0.0%)	1.4% (-0.5%, 3.3%)	2 (1.1%)
Anti-Hypertensive	4 (2.8%)	2 (1.6%)	1.2% (-2.2%, 4.7%)	2 (1.1%)
Anti-Platelet	10 (7.0%)	2 (1.6%)	5.4% (0.7%, 10.1%)	18 (9.5%)
Diuretic	5 (3.5%)	5 (3.9%)	-0.4% (-4.9%, 4.1%)	3 (1.6%)
Other	36 (25.2%)	29 (22.7%)	2.5% (-7.6%, 12.7%)	55 (29.1%)

NOTE: Analysis includes all Feasibility subjects, non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006 and evaluated through 12 month follow-up.

[1] Differences between Pivotal device and surgery groups and associated 95% confidence intervals.

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GORE HELEX SEPTAL OCCLUDER

Design

PIVOTAL STUDY

The Multicenter Pivotal Study of the GORE HELEX Septal Occluder was a non-randomized, controlled trial comparing safety and efficacy outcomes of the GORE HELEX Septal Occluder with traditional (open) surgical repair of atrial septal defects.

The primary study endpoint was clinical success, a composite evaluation of safety and efficacy, which was evaluated at 12 months post-procedure. Clinical success was defined as: 1) A residual defect classified as either completely occluded or clinically insignificant leak as determined by echocardiography core lab assessment; 2) No repeat procedure to the target ASD; and 3) No major device- or procedure-related adverse events. The study was designed to demonstrate that the clinical success rate of the GORE HELEX Septal Occluder was not inferior to the clinical success rate for surgical closure of ASDs.

Additional safety endpoints included the proportion of subjects experiencing one or more major and minor device-related and / or procedure-related adverse events through 12 months post-procedure. Additional efficacy endpoints included delivery (technical) success, defined as successful deployment and accurate placement of the GORE HELEX Septal Occluder to the target ASD, and treatment efficacy, defined as the proportion of subjects with a final residual defect assessment of clinically successful closure (completely occluded or clinically insignificant leak).

CONTINUED ACCESS STUDY

The Continued Access Study was a prospective, single-arm trial intended to evaluate design modifications to the GORE HELEX Septal Occluder. The design modifications incorporated into the GORE HELEX Septal Occluder were implemented based on investigator input and feedback given during the Feasibility and Pivotal Trials. The Continued Access Study endpoints were the same as those of the Pivotal Study and were evaluated at 12 months.

Method

PIVOTAL STUDY — DEVICE TREATMENT ARM

For patients enrolled in the device treatment arm of the Pivotal Study, dimensional verification and characterization of the ASD and surrounding cardiac structures were performed per the investigator's standard methods. An initial static measurement of the septal defect was obtained during echocardiographic visualization. A second measurement was taken utilizing a balloon to gently stretch the defect and measure the balloon's waist (narrowest portion of the balloon), and the balloon stretched defect size was used to determine the optimal size of the GORE HELEX Septal Occluder per IFU recommendations. Fluoroscopic and echocardiographic guidance were used throughout the procedure for placement of, and at the completion of each procedure to assess the status of, the GORE HELEX Septal Occluder.

There was no requirement for prior therapy or medical management. All subjects were placed on the investigator's choice of antiplatelet therapy for six months following implantation of the GORE HELEX Septal Occluder, and on prophylactic, post-procedure antibiotic therapy consistent with the investigator's routine procedure.

Follow-up evaluations, which included a physical exam, ECG, and an assessment of the residual defect status by TTE, were performed at hospital discharge, and at 1, 6, and 12 months post-procedure. If the TTE was inconclusive, a TEE or angiography may have been performed. At the 6 and 12 month follow-up visits, fluoroscopic examinations were performed to assess device integrity.

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Method

PIVOTAL STUDY — SURGICAL CONTROL ARM

Investigators identified surgical control subjects at their respective sites who had undergone an open-heart surgical ASD closure within 12 months of IRB approval of the Pivotal Study, and who also met the inclusion / exclusion criteria for the control arm. Open-heart surgical ASD repair was performed per the investigator's standard procedure, and was achieved by suturing the defect edges or by implantation of autologous or synthetic patch materials over the defect.

Subjects were placed on antiplatelet therapy and prophylactic, post-procedure antibiotic therapy at the investigator's discretion and consistent with investigator's standard method.

Follow-up evaluations, which included a physical exam, ECG, and an assessment of the residual defect status by TTE, were performed at hospital discharge and at 12 months. If the TTE was inconclusive, a TEE or angiography may have been performed.

CONTINUED ACCESS STUDY

The methodology and follow-up of the Continued Access Study was the same as that of the device treatment arm of the Pivotal Study.

Results

PIVOTAL STUDY — DEVICE TREATMENT ARM

The GORE HELEX Septal Occluder was successfully implanted in 88.1% (119 / 135) of subjects with a delivery attempt. No deaths, device-related thrombus, perforations, or erosions requiring surgery were reported. Major adverse events were reported in 5.9% of subjects with a successful delivery through the 12 month follow-up. Clinically successful closure (complete occlusion or clinically insignificant leak), as determined by echocardiographic core laboratory review, was achieved in 98.1% of subjects evaluated at 12 months post-procedure. The primary clinical success endpoint was achieved in 91.7% of subjects evaluated.

PIVOTAL STUDY — SURGICAL CONTROL ARM

Major adverse events were reported in 10.9% of control subjects. One death resulting from complications of post-pericardiotomy syndrome was reported. Clinically successful closure, as determined by echocardiographic core laboratory review, was achieved in 100% of subjects evaluated at 12 months post-procedure. Clinical success was achieved in 83.7% of subjects evaluated.

CONTINUED ACCESS STUDY

The GORE HELEX Septal Occluder was successfully implanted in 85.6% of subjects with an attempt. No deaths, device-related thrombus, perforations, or erosions requiring surgery were reported. Major adverse events were reported in 2.2% of subjects with a successful delivery who have been evaluated through 12 months. Clinically successful closure, as determined by echocardiographic core laboratory review, was achieved in 99.1% of subjects who have been evaluated at 12 months post-procedure. The primary clinical success endpoint was achieved in 96.7% of subjects evaluated.

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Tables of Safety and Effectiveness Results

The principal safety and effectiveness results through 12 months and the procedure outcomes for the Pivotal and Continued Access Studies are reported in Tables G-6 and G-7.

Table G-6

GORE HELEX Septal Occluder Studies — Principal Safety and Effectiveness Results				
	Pivotal Study			Continued Access Study
Study Outcomes	Device Arm	Surgery Arm	Difference (95% CI)[4]	
Technical Success[1]	**119 / 135 (88.1%)**	**n / a**	**n / a**	**137 / 160 (85.6%)**
Clinical Closure Success[2]				
Pre-Discharge	115 / 118 (97.5%)	128 / 128 (100%)	-2.5% (-5.4%, 0.3%)	134 / 136 (98.5%)
Month 6	99 / 101 (98.0%)	n / a	n / a	111 / 111 (100%)
Month 12	103 / 105 (98.1%)	82 / 82 (100%)	-1.9% (-4.5%, 0.7%)	116 / 117 (99.1%)
Principal Safety Measures				
Major Adverse Events 12 Months	7 / 119 (5.9%)	14 / 128 (10.9%)	-5.1% (-11.9%, 1.8%)	3 / 137 (2.2%)
Minor Adverse Events 12 Months	34 / 119 (28.6%)	36 / 128 (28.1%)	0.4% (-10.8%, 11.7%)	46 / 137 (33.6%)
Survival at 365 Days (K-M)	100%	99.2%	-0.8% (-2.3%, 0.7%)	100%
Composite Clinical Success 12 Months[3]	**100 / 109 (91.7%)**	**72 / 86 (83.7%)**	**8.0% (-1.3%, 17.2%)**	**116 / 120 (96.7%)**

NOTE: Analysis includes all non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006 and evaluated through 12 month follow-up.
n / a: Not applicable.
[1] Technical Success defined as successful delivery of the device in subjects with a delivery attempted.
[2] Clinical Closure Success defined as residual defect that is either Completely Occluded or Clinically Insignificant Leak.
Leak status was evaluated by the investigational sites at pre-discharge and six months and by the echocardiography core laboratory at 12 months.
[3] Composite Clinical Success defined as no major adverse event or repeated procedure and clinical closure success at 12 months.
[4] Differences between Pivotal device and surgery groups and associated 95% confidence intervals.

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GORE HELEX SEPTAL OCCLUDER

Tables of Safety and Effectiveness Results

Table G-7

GORE HELEX Septal Occluder Studies — Procedural Outcomes				
	Pivotal Study			Continued Access Study
	Device Arm	Surgery Arm	Difference (95% CI)[1]	
Subjects with Delivery Attempt / Surgery	**135**	**128**		**160**
Total Time Under Fluoroscopy (minutes)				
N	134	n / a		155
Mean (Std Dev)	28 (21)			23 (16)
Median	22			19
Range	(6, 148)			(5, 116)
Total Time Under Anesthesia (minutes)				
N	133	128		155
Mean (Std Dev)	168 (63)	205 (43)	-37.1 (-50.3, -23.9)	153 (63)
Median	160	202		150
Range	(55, 360)	(30, 330)		(0, 380)
Days in Hospital for Procedure				
N	135	128		160
Mean (Std Dev)	1 (0)	3 (1)	-1.9 (-2.1, -1.7)	1 (0)
Median	1	3		1
Range	(0, 4)	(1,9)		(0, 2)

NOTE: Analysis includes all non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006.
n / a: Not applicable.
[1] Differences between Pivotal device and surgery groups and associated 95% confidence intervals.

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Attempted and Delivered

Table G-8 presents the number of devices attempted and number of those successfully delivered for each device size overall and by subject age at procedure for combined device subjects from the Pivotal and Continued Access Studies.

Table G-8

GORE HELEX Septal Occluder Studies Number of Devices Attempted and Successfully Delivered By Device Size and Subject Age at Procedure						
GORE HELEX Septal Occluder Device Size	15 mm (N_S/N_A)[1]	20 mm (N_S/N_A)[1]	25 mm (N_S/N_A)[1]	30 mm (N_S/N_A)[1]	35 mm (N_S/N_A)[1]	Overall (N_S/N_A)[1]
Subject Age						
Infant (< 2 yrs)	1 / 1	3 / 3	3 / 9	0	0	7 / 13
Child (2 – 5 yrs)	5 / 5	23 / 32	58 / 108	30 / 71	4 / 21	120 / 237
Child (6 – 11 yrs)	3 / 3	11 / 13	17 / 24	23 / 42	4 / 16	58 / 98
Adolescent (12 – 20 yrs)	2 / 2	8 / 11	13 / 18	11 / 16	13 / 24	47 / 71
Adult (21+ yrs)	0	1 / 1	5 / 5	7 / 8	11 / 18	24 / 32
Overall	**11 / 11**	**46 / 60**	**96 / 164**	**71 / 137**	**32 / 79**	**256 / 451**

NOTE: Analysis includes all non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006.
[1] N_S = Number of successful device deliveries. N_A = Number of devices attempted.

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Summary of Reported Medications for Device Subjects

Table G-9 presents the frequency of reported medications at follow-up visits for combined device subjects from the Pivotal and Continued Access Studies.

Table G-9

GORE HELEX Septal Occluder Studies Summary of Reported Medications for Device Subjects				
MEDICATIONS	PRE-PROCEDURE	PRE-DISCHARGE	6 MONTHS	12 MONTHS
Anti-Platelet	28 / 333 (8.4%)	224 / 255 (87.8%)	147 / 215 (68.4%)	21 / 236 (8.9%)
Anti-Arrhythmic	7 / 333 (2.1%)	6 / 255 (2.4%)	5 / 215 (2.3%)	4 / 236 (1.7%)
Anti-Hypertensive	6 / 333 (1.8%)	4 / 255 (1.6%)	3 / 215 (1.4%)	4 / 236 (1.7%)
Anti-Coagulant	4 / 333 (1.2%)	13 / 255 (5.1%)	2 / 215 (0.9%)	4 / 236 (1.7%)
Diuretic	8 / 333 (2.4%)	2 /255 (0.8%)	2/ 215 (0.9%)	2 / 236 (0.8%)

NOTE: Analysis includes all non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006.

Summary of Procedural Fluoroscopy Times

Table G-10 presents a summary of procedural fluoroscopy time by device delivery success and number of devices attempted for combined device subjects from the Pivotal and Continued Access Studies.

Table G-10

GORE HELEX Septal Occluder Studies Summary of Procedural Fluoroscopy Times for Device Subjects			
	N	MEDIAN (MINUTES)	RANGE (MINUTES)
Subjects with Successful Delivery	**256**	**18.6**	**(5.3, 92.1)**
One Device Attempted	178	15.1	(5.3, 46.6)
Two Devices Attempted	54	28.9	(9.8, 76.1)
Three or More Devices Attempted	24	39.7	(24.0, 92.1)
Subjects with Unsuccessful Delivery	**39**	**36.0**	**(13.4, 148.0)**
One Device Attempted	19	26.3	(13.4, 51.3)
Two Devices Attempted	9	34.9	(31.3, 56.2)
Three or More Devices Attempted	11	74.2	(41.5, 148.0)

NOTE: Analysis includes all non-training Pivotal subjects and Continued Access subjects enrolled as of 08/01/2006.

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Conclusion

The clinical success outcomes satisfied the primary, non-inferiority hypothesis for the Pivotal Study ($p < 0.001$ using two-sample binomial proportions test with non-inferiority margin of 10%) and indicated that the clinical success rate of the GORE HELEX Septal Occluder is not inferior to surgical closure.

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